1626

Attorney Docket No. IVD 0048

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Franc et al.

U.S. Appln. Serial No.: 09/720,017

Filing Date: 03/12/01

Group Art Unit: 1626

Examiner: Sonya N. Wright

For: NOVEL FORM OF IRBESARTAN, METHODS FOR OBTAINING SAID FORM AND PHARMACEUTICAL COMPOSITIONS CONTAINING SAME

CERTIFICATE UNDER 37 C.F.R. 1.8(a)

I hereby certify that this correspondence is being deposited on the date indicated below with the United States Postal Service as first class mail addressed to: Commissioner for Patents, Washington, D.C. 20231

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Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

RESPONSE AND AMENDMENT

This is in response to the Office Action mailed on August 14, 2002 by the United States Patent and Trademark Office setting a three-month period for response which was set to expire on November 14, 2002. The three-month shortened statutory period for response is hereby extended by three months to February 14, 2003 pursuant to the Petition for Extension of Time under 37 C.F.R. §1.136(a) which is submitted herewith.

The telephonic requirement for restriction between Groups I-VI:

Group I:	Claims 1-3, 28-30 and 41-42
Group II:	Claims 4 and 35-40
Group III:	Claim 5-19
Group IV:	Claims 20-27
Group V:	Claims 31-34
Group VI:	Claims 43-45

by the Examiner on August 1, 2002 and applicants' election, with traverse, of the subject matter of Group I, claims 1-3, 28-30 and 41-42 is hereby acknowledged. The requirement for restriction is traversed and reconsideration and modification thereof are requested for the reasons given hereinbelow.

Initially, applicants would point out that the subject matter of Groups I-VI are simply different aspects of the same inventive concept and should, therefore, be considered a single invention and not "two or more independent and distinct inventions" within the meaning of 35 U.S.C. §121. Furthermore, as set forth at the bottom of page 2 of the instant Office Action:

> The method for determining unity of invention under Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:
> (i) in addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product.

Accordingly, at the very least, the subject matter of Group I as well as the subject matter of Group II (a process for the manufacture of said product) and Group VI (a use of said product) should be considered to comply with the unity of invention requirement.

Claims 1-30 were in the application as filed. Claims 31-45 were added in the Preliminary Amendment dated December 19, 2000. Claims 1-45 remain in the application.

Claims 1-3, 28 and 41-42 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,629,331 to Caron et al. In support of this rejection the Examiner has stated that:

> Caron et al. teach crystalline forms of 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one compounds and their use as pharmaceuticals. Applicant discloses a crystalline 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one

> compound and its use as a pharmaceutical. Caron et al. teach 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one in column 1, lines 40-47. Crystalline forms of 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one and pharmaceutical compositions containing the crystalline form are taught in column 1, lines 10-12.
>
> The instant claims include the ratio between the length and the width of the crystals in the claimed compound. The Caron et al. reference differs from the instant claims because Caron et al. do not include the ratio between the length and the width of the crystals.
>
> However, specifying the ratio between the length and width of crystals is an obvious variation absent a showing of unexpected results (see In re Grose and Flanigen, 201 USPQ 57, CCPA 1979). Further, the instant crystalline compounds have the same utility as the crystalline compounds of Caron et al. (see In re Weijard, 1946 C.D. 175, 69 USPQ 86). One of ordinary skill in the art would be motivated [sic, to] use the teachings of Caron et al. in the expectation that varying lengths and widths of crystals would improve the usefulness of the compound in pharmaceuticals.

This rejection is traversed and reconsideration and withdrawal thereof are requested for the reasons given hereinbelow.

Caron et al., disclose a process for preparing two different crystalline forms, Forms A and B, of 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one. Form A is described as being in the form of stable, non-hygroscopic needles of high electrostatic nature in which the hydrogen atom of the tetrazole ring is in the 1-position. Form B is described as being constituted by triclinic crystals of the tautomer having the hydrogen atom of the tetrazole ring in the 2-position (see column 3, lines 3-15 of Caron et al.). The instantly claimed invention, on the other hand, is directed to a novel crystalline habit of Form A of irbesartan wherein the ratio between the length and the width of the crystals is between 1:1 and 10:1 and to processes for preparing the same.

Initially, applicants would point out that on page 2, lines 15-23 of the instant application is stated that the acicular crystal habit of Form A which is described in EP

708103 (corresponds to U.S. Patent No. 5,629,331) is difficult to filter and dry, displays poor flowability and has a high electrostatic nature. What applicants have unexpectedly discovered is that the instantly claimed novel crystal habit of irbesartan has less of a tendency to break or to aggregate when wet, it can be filtered and dried faster and it is easier to handle when it is dry than the acicular crystal habit of Form A described in Caron et al. Of particular note in this regard is the unexpected discovery that (a) the chargeability of the instantly claimed crystal habit of irbesartan was only between 0-10 nanocoulomb/g, compared to the acicular crystal habit of Form A which was –30 to –40 nanocoulomb/g, which indicates that the instantly claimed crystal habit of irbesartan has a substantially reduced tendency to store electrostatic charges and can be handled more easily and safely, and (b) the packing density of the instantly claimed crystal habit of irbesartan was approximately 50% greater (0.5 kg/m^3 versus 0.35 kg/m^3) than that for Form A of Caron et al., and the flowability index was 3 times greater (30 versus 10) than that for Form A of Caron et al., which means that the chemical processability of the instantly claimed crystal habit of irbesartan will be substantially improved. Accordingly, the instantly claimed novel crystal habit of irbesartan surprisingly solved each of the problems associated with Form A of Caron et al., i.e., highly electrostatic in nature, difficult to filter and dry and displays poor flowability.

Surely it can not be said that there is any disclosure contained in Caron et al., which could possibly teach or suggest to one skilled in the art that irbesartan could even exist in another crystal habit other than the two disclosed in Caron et al., let alone that such a novel crystal habit, if discovered, would surprisingly solve all of the problems associated with the prior art crystal habit of Form A. Accordingly, contrary to the Examiner's assertion, the disclosure contained in Caron et al., would have provided absolutely no motivation for one of ordinary skill in the art to vary the length and width of the prior art crystals of irbesartan let alone to develop a crystal habit of irbesartan with the specific ratios specified in the instant claims. Thus, it is submitted that the Caron et al., reference is inadequate to render applicants' claimed invention obvious. Neither Caron et al, nor any other references of which applicants are aware has any teaching or suggestion which would have led a person of ordinary skill in the art to applicants' claimed invention. The claimed invention would, therefore, not have

been obvious to such a person at the time the invention was made and, hence, the rejection of claims 1-3, 28, and 41-42 based on said reference is believed to be unwarranted and should be withdrawn.

In view of the foregoing remarks, reconsideration and withdrawal of the restriction requirement and the rejection of claims 1-3, 28, and 41-42 is requested and allowance of claims 1-45 is respectfully requested.

Respectfully submitted,

Date: February 5, 2003

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